Claim 27. The immunostimulating composition of claim 15, wherein the size of more than 50% (by volume) of the vaccine microspheres is between 5 and 10 μm in diameter.

Claim 28. The immunostimulating composition of claim 15, wherein said immunostimulating composition is administered as a mucosal vaccine or a parenteral vaccine.

Claim 29. The immunostimulating composition of claim 28 in the form of a mucosal administerable vaccine wherein the diameter size range of the vaccine microspheres is between 5-10μm.

Claim 30. The immunostimulating composition of claim 28 in the form of a parenteral administerable vaccine wherein the diameter size range of the vaccine microspheres is between 0.1 - 20μm.

Claim 31. The immunostimulating composition of claim 30, wherein said immunogenic substance is present in an amount of 0.5 - 5% antigen by weight.

Claim 32. The immunostimulating composition of claim 15, wherein said bulk matrix encapsulates said immunogenic substance protectively and/or facilitates its interaction with the host immune system to augment its immunogenicity.

Claim 33. A vaccine comprising the immunostimulating composition of claim 15.

REMARKS

The specification has been amended at column 5 to correct typographical errors. Support for the amendment to column 5 is found in the figures.

The spelling of the inventor, Deborah Birx has been corrected.

The figure description in column 2 beginning at line 13 of FIG. 1 has been amended to correct an inadvertent inaccuracy. Support for this amendment is found in the Figure 1 and in column 2, line 27.

The specification has been amended at column 2, in the paragraph beginning at line 19 to include the molecular weight range of the polymer. Support for this amendment is found in the originally submitted claims 1 and 6.

The specification has been amended at column 2, in the paragraph beginning at line 46 to insert ---1 nanometer --- to indicate the lower range of microsphere diameter and to indicate an amount of immunogenic substance of 0.5% to 5.0% of the weight of the composition. Support for these amendments is found in the originally submitted claims 4 and 8.

Claims 7 and 11 have been amended to correct improper multiple dependencies and to change the term "consisting of" to --- comprising ---. Claims 8, 12 and 13 have been amended to correct spelling errors.

New claims 15-33 are supported by claims 1-14 and the description as originally filed. No new matter has been added.

A marked up specification showing insertions with underlining and deletions with bracketing is submitted herewith in accordance with 37 CFR §1.173.

Respectfully submitted:

Date: June 2, 2000

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Please add claims 15-33 as follows:

Claim 15. An immunostimulating composition comprising encapsulating microspheres, wherein said encapsulating microspheres comprise:

a biodegradable-biocompatible poly(DL-lactide-co-glycolide) as a bulk matrix and

an immunogenic substance comprising a conformationally native subunit of chronic intracellular pathogen which, in the course of natural infection with that pathogen, is exposed to the host immune system on the surface of free pathogen and/or pathogen-infected cells.

Claim 16. The immunostimulating composition of claim 15, wherein the encapsulating microspheres are produced by a solvent extraction process.

Claim 17. The immunostimulating composition of claim 15, wherein the encapsulating microspheres are produced by a solvent evaporation process.

Claim 18. The immunostimulating composition of claim 15, wherein the antigen is pre-encapsulated into a conformationally stabilizing hydrophilic matrix comprising an appropriate mono, di- or tri-saccharide or other carbohydrate substance by lyophilization prior to its final encapsulation into the PLG microsphere.

Claim 19. The immunostimulating composition of claim 18, wherein the encapsulating microspheres are produced by a solvent extraction process.

Claim 20. The immunostimulating composition of claim 19, wherein said solvent extraction process employs acetonitrile as the polymer solvent, mineral oil as the emulsion's external phase, and heptane as the extractant.

Claim 21. The immunostimulating composition of claim 15, wherein said microspheres further comprise a pharmaceutically acceptable adjuvant.

Claim 22. The immunostimulating composition of claim 15, wherein a molecular weight of the poly(DL-lactide-co-glycolide) is 4,000 to 100,000 daltons.

Claim 23. The immunostimulating composition of claim 15, wherein the relative ratio between the amount of the lactide:glycolide components of the matrix is within the range of 52:48 to 0:100.

Claim 24. The immunostimulating composition of claim 15, wherein the immunogenic substance is a native (oligomeric)HIV-1 envelope antigen.

Claim 25. The immunostimulating composition of claim 15, wherein the amount of said immunogenic substance with in the microsphere comprises between 0.5% to 5.0% of the weight of said composition.

Claim 26. The immunostimulating composition of claim 15, wherein the diameter size range of the microspheres is between 0.1 - 20μm.

Claim 27. The immunostimulating composition of claim 15, wherein the size of more than 50% (by volume) of the vaccine microspheres is between 5 and 10 μm in diameter.

Claim 28. The immunostimulating composition of claim 15, wherein said immunostimulating composition is administered as a mucosal vaccine or a parenteral vaccine.

Claim 29. The immunostimulating composition of claim 28 in the form of a mucosal administerable vaccine wherein the diameter size range of the vaccine microspheres is between 5-10μm.

Claim 30. The immunostimulating composition of claim 28 in the form of a parenteral administerable vaccine wherein the diameter size range of the vaccine microspheres is between 0.1 - 20μm.

Claim 31. The immunostimulating composition of claim 30, wherein said immunogenic substance is present in an amount of 0.5 - 5% antigen by weight.

Claim 32. The immunostimulating composition of claim 15, wherein said bulk matrix encapsulates said immunogenic substance protectively and/or facilitates its interaction with the host immune system to augment its immunogenicity.

Claim 33. A vaccine comprising the immunostimulating composition of claim 15.